**DOCKET NO.:** NIHB-2428 **PATENT** 

**Application No.:** 10/789,400

Office Action Dated: March 9, 2009

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:** 

1. (Currently Amended) An attenuated, replication competent recombinant human

metapneumovirus (rHMPV), comprising a partial or complete, recombinant HMPV genome

or antigenome comprising one or more attenuating nucleotide modifications including a

partial or complete deletion of theone or more rHMPV-SH, G, M.2-1, M2-2, or M2 ORFs or

one or more nucleotide substitutions that reduces or ablates expression of the one or more

rHMPV-SH, G, M2-1, M2-2, or M2 ORFs, and

a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), and a large

polymerase protein (L) of a HMPV.

2. (Canceled)

3. (Original) The rHMPV of claim 1, wherein the recombinant HMPV genome or

antigenome further comprises a detectable heterologous sequence encoding a polypeptide.

4. (Original) The rHMPV of claim 3, wherein the detectable heterologous sequence

encodes a reporter.

5. (Original) The rHMPV of claim 4, wherein the reporter comprises green

fluorescent protein (GFP).

6. (Previously Presented) The rHMPV of claim 3, wherein the detectable heterologous

sequence is operably linked to a HMPV gene transcription start signal and to a HMPV gene

end signal.

7.-14. (Canceled).

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15. (Currently Amended) The rHMPV claim 1, wherein the one or more attenuating nucleotide modifications comprises one or more nucleotide substitutions that reduces or ablates expression of a rHMPV M2-2 ORF.

- 16. (Currently Amended) The rHMPV of claim 15, wherein the one or more nucleotide substitutions that reduces or ablates expression of the rHMPV M2-2 ORF comprises one or more nucleotide substitutions that ablates one or more potential translation initiation codons of the rHMPV M2-2 ORF or introduces one or more in-frame stop codons into the rHMPV M2-2 ORF.
- 17. (Previously Presented) The rHMPV of claim 16, wherein the one or more nucleotide substitutions comprises substitutions of one or more nucleotides of the sequence set forth as SEQ ID NO: 1.
- 18. (Previously Presented) The rHMPV of claim 1, wherein the one or more attenuating nucleotide modifications comprises a partial or complete deletion of a rHMPV M2-2 ORF, such that a wild type M2-2 protein is not produced.
- 19. (Previously Presented) The rHMPV of claim 1, wherein the one or more attenuating nucleotide modifications comprises a partial or complete deletion of a M2-2 ORF of SEQ ID NO: 1.

20.-24. (Cancelled)

25. (Previously Presented) The rHMPV of claim 1, wherein the one or more attenuating nucleotide modifications produces at least one desired phenotypic change in the rHMPV, wherein the phenotypic change comprises at least one change selected from the group consisting of a change in growth properties in cell culture, a change in growth properties or virulence in the upper or lower respiratory tract of a mammalian host, a change in viral plaque size, a change in sensitivity or adaptation to temperature, a change in cytopathic effect, a change in the efficiency of transcription or genome replication, a change

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in sensitivity to interferon, a change in the efficiency of expression of one or more genes and

a change in immunogenicity.

26. (Currently Amended) The rHMPV of claim 25, wherein the one or more

attenuating nucleotide modifications produces a change in viral growth in the upper

respiratory tract, lower respiratory tract, or both, such that viral growth is attenuated by about

<del>50-1 00-50-100</del> fold or greater, compared to growth of the corresponding wild type HMPV

strain.

27.-57. (Cancelled)

58. (Previously Presented) The rHMPV of claim 16, that demonstrates a ten-fold or

more reduction in growth in the presence of interferon, but is not attenuated when growing in

the absence of interferon.

59. (Previously Presented) The rHMPV of claim 18, that demonstrates a ten-fold or

more reduction in growth in the presence of interferon, but is not attenuated when growing in

the absence of interferon.

60.-61. (Cancelled)

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